UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JUL 8 1998

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Registration of Fortune Aza Technical Containing 14.5% Azadirachtin A and B (File Symbol 71038-G, Chemical No. 121701). Review of Mammalian Toxicity Data (MRID 443663-08; Submission S536011; DP Barcode D242249).

FROM: Sheryl K. Reilly, Ph.D., Senior Scientist
Biochemical Pesticides Branch
Biopesticides and Pollution Prevention Division (7511C)

TO: Rita Kumar, Regulatory Action Leader
Biochemical Pesticides Branch
Biopesticides and Pollution Prevention Division (7511C)

ACTION REQUESTED: Review of a dermal sensitization study for Fortune Aza Technical, (File Symbol 71038-G), a biochemical insecticide.

CONCLUSIONS AND RECOMMENDATIONS: This product is a dermal sensitizer when tested by the method of Magnussen and Kligman (guinea pig maximization test). The study is acceptable and was performed in accordance to the guideline for dermal sensitization studies (152-15/81-6). The product label should include an appropriate precautionary statement that sensitive individuals may exhibit an allergic skin reaction to this product, if repeated skin contact is expected based upon the use of this technical product. If personal protective clothing is worn or skin exposure is otherwise not anticipated to be significant, this statement may be omitted.

The Data Evaluation Report for this study is attached.

DATA EVALUATION REPORT

AZADIRACHTIN
(FORTUNE AZA TECHNICAL)

STUDY TYPE: DERMAL SENSITIZATION - GUINEA PIG (81-6)

Prepared for

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Office of Pesticide Programs
U.S. Environmental Protection Agency
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Prepared by

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Task Order No. 20

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Date: 4-23-98

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Signature: L. A. Wilson
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Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory, managed by Lockheed Martin Energy Research Corp. for the U.S. Department of Energy under contract number DE-AC05-96OR22464.

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (§81-6, 870.2600)

EPA Reviewer: Sheryl K. Reilly, Ph.D. Sheryl K Reilly Date 7/8/98
Biopesticides and Pollution Prevention Division (7511C)

MRID No.: 443663-08
DP Barcode: D242249
Study No.: FBT 10/952234/SS
Submission: S536011
Study Completion Date: July 3, 1997

Testing Facility: Huntingdon Life Sciences Ltd.
Authors: Allan, S. and Coleman, D.

Quality Assurance (40 CFR §160.12): Included
Compliance with Good Laboratory Practice Standards: Yes, statement dated July 28, 1997

Test Material: Fortune AZA Technical (Reported to be 8.5% Azadirachtin; later demonstrated to be 14.5% Azadirachtin; see MRIDs 443663-01 and -02, and 443967-01); Batch 0010195-0050195; brown powder
Positive Control Material: Hexyl cinnamic aldehyde (Historical data)
Species: Guinea pigs; Albino, Dunkin/Hartley
Age: 5-6 weeks at the start of the study (after 6 days of acclimation)
Weight: Males: 363-426 g at the start of the study
Source: D. Hall, Newchurch, Staffordshire, England
Method: Maximization Test

Conclusion: This product **is a dermal sensitizer** when tested by the method of Magnussen and Kligman (guinea pig maximization test). The study is acceptable.

Procedure (§81-6): The sensitivity of the guinea pig strain used in the present study is checked periodically at the performing laboratory with hexyl cinnamic aldehyde (HCA) via the method of Magnussen and Kligman. The historical data presented in the study report were appropriate.

***Procedure**: In a preliminary dose range-finding study, the intradermal and topical irritancies of a* range of dilutions of test material were investigated (in Alembicol D). All animals were pretreated with an intradermal injection of Freund's complete adjuvant (50:50 in water) one week prior to the start of the preliminary study. Intradermal injections (0.1 mL/dose) were made into the clipped flank of 2 test animals, and the reactions were assessed at 24 and 72 hours post injection. For topical applications, 20 x 20 mm patches of Whatman No. 3 filter paper were saturated with each concentration of test material and applied to the shaved skin on the flanks of each of 4 guinea pigs. The patches were covered with an occlusive tape and removed after 24 hours. The reaction sites were assessed for irritation at 24 and 72 hours following the removal of the patches. The dose selected for intradermal induction was 0.5% w/v in Alembicol D, the highest concentration of test material that caused irritation but otherwise did not adversely affect the test animals. The dose selected for the topical inductions was 60% w/v in Alembicol D (the maximum dose that did not give rise to topical irritation), and 60% and 30% w/v were chosen for the topical challenge phase of the study. .

For the induction phase of the study, 3 pairs of intradermal injections (0.1 mL/site) were made into a 20 x 40 mm area within a 40 x 60 mm area of shaved dorsal skin on the scapular region of the guinea pigs. The injectables were (1) Freund's complete adjuvant (diluted with equal volume of water), (2) 0.5% w/v test material in Alembicol D, and (3) 0.5% w/v test material in 50:50 mixture

of Freund's complete adjuvant and Alembicol D. Six days later, the same scapular region was clipped and treated with 0.5 mL/site of 10% w/w sodium lauryl sulfate in petrolatum. Twenty four hours later, the animals were treated topically at the same skin site with 0.4 mL of 60% w/v test material in Alembicol D (applied to Whatman No. 3 filter paper patches) under occlusion for 48 hours. Evaluation after each induction was reported by group. The naive control animals were treated similarly to the test animals with the exception that the test material was omitted from the intradermal injections and topical application.

Two weeks after the topical induction, the left flanks of the test and control animals were clipped and topically challenged (using Whatman No. 3 filter paper patches) with 0.2 mL of 60% w/v test material in Alembicol D and 0.2 mL of 30% w/v test material in Alembicol D at a more posterior site for 24 hours. The sites were evaluated 24, 48, and 72 hours after removal of the patches.

Results: Intradermal necrosis was noted on all of the test animals following treatment with Freund's complete adjuvant and 0.5% w/v test material in 50:50 mixture of Freund's complete adjuvant and Alembicol D and on all of the naive control animals following treatment with Freund's complete adjuvant and 50:50 mixture of Freund's complete adjuvant and Alembicol D. The test animals intradermally induced with 0.5% w/v test material in Alembicol D and the naive control animals induced with Alembicol D had slight irritation at those injection sites. All of the test animals had moderate erythema and all naive control animals exhibited slight erythema after topical induction. Following topical challenge, all test animals had slight to well defined erythema with or without slight edema 24, 48, and 72 hours after patch removal at both the 60% and 30% challenge sites. Dermal irritation was not observed in the naive control animals after topical challenge. The test substance was positive for dermal sensitization in this study.

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